

# WGCAC Computational Systems Biology for Complex Human Disease 4-9 December 2022

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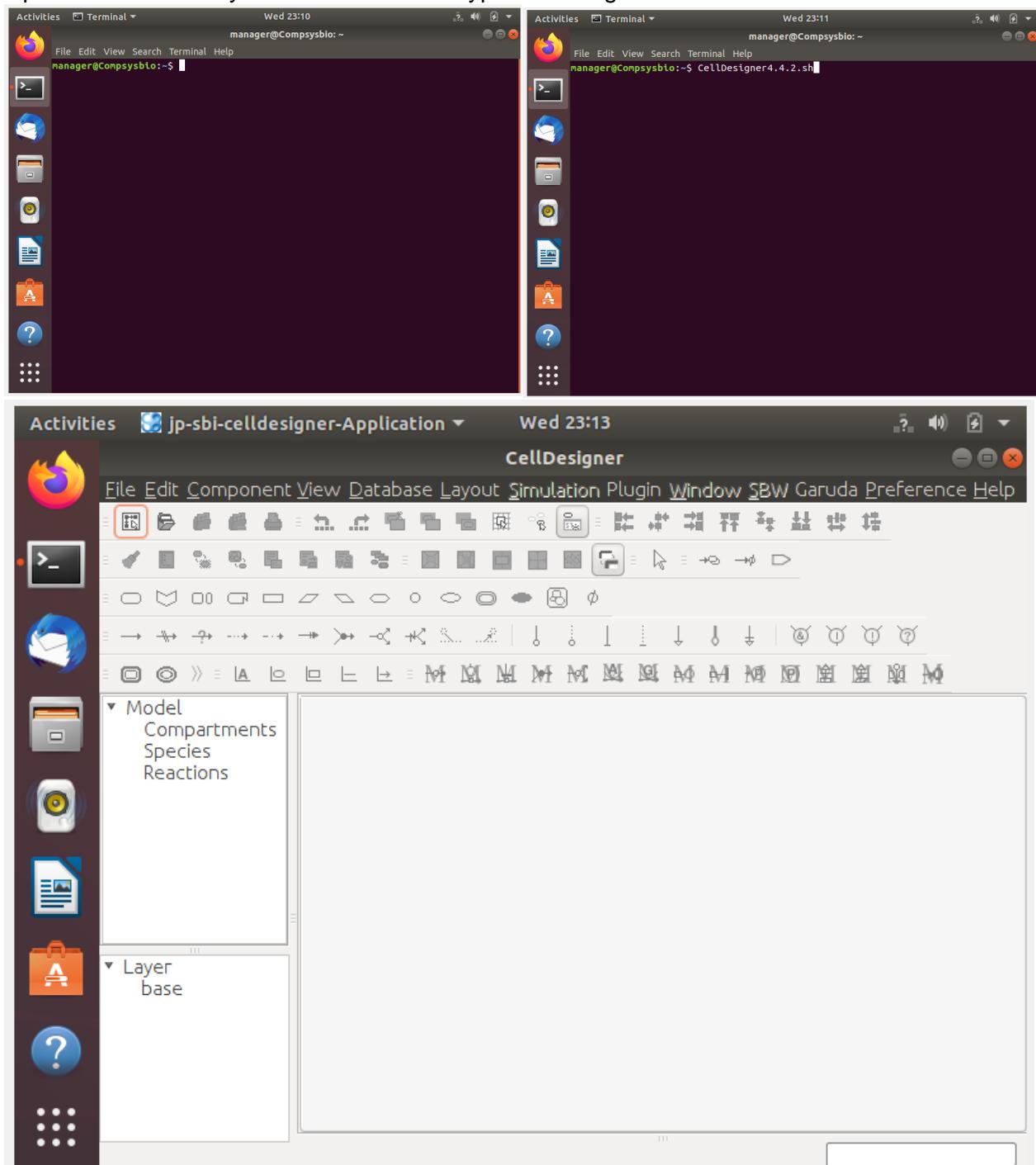
## Hands-on session with CellDesigner

In this session, we are going to see examples of CellDesigner diagram functionalities. We will also open and observe a file containing a graphical model of apoptosis.

The functionalities we will see are summarized below:

Open a new model	Create a reaction	Add anchor point	Add catalytic reaction	Set active state
Change color	Include compartment	Add residue to protein	Change position of residue	Create complex
Include genes and RNAs	Connect to databases	Choose layout		

Open the terminal in your VM session and type CellDesigner4.4.2.sh



You will see in your screen the general view as discussed in the demo:

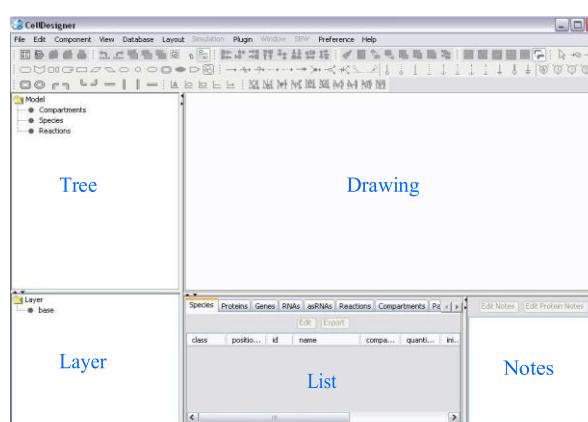
## General view

**TREE AREA**  
displays all the list of the components in a tree structure.

**DRAW AREA**  
is the area where the model is built from the tool bar items.

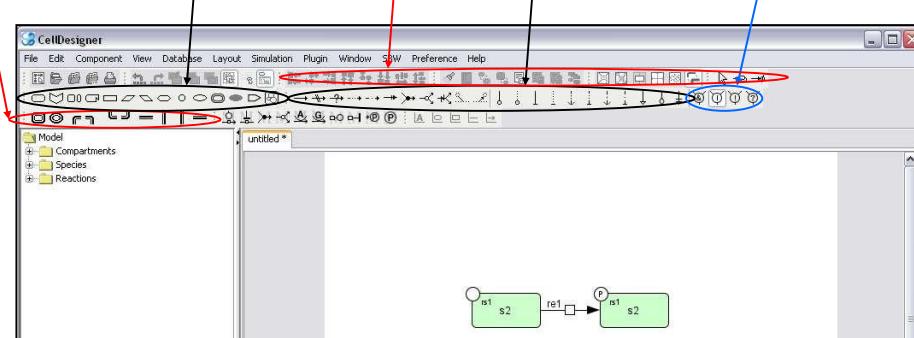
**LIST AREA**  
displays and edits the list of the components of the model (species, proteins, genes, RNAs, etc.)

**NOTES AREA**  
displays and edits the notes of each component (reactions, protein, complex, etc.)



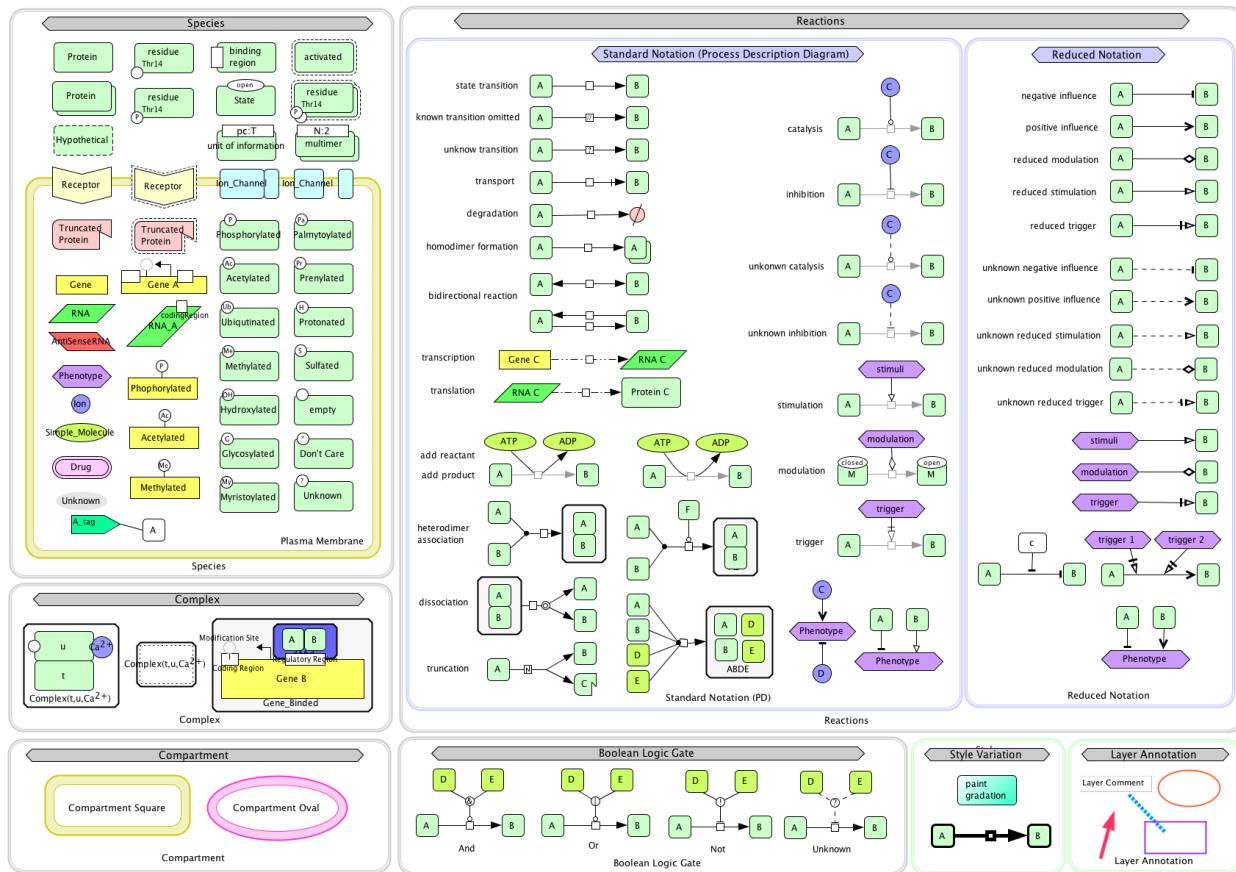
Take some time to explore the menu. Check the glyphs, the arcs and the macros. Highlighted below the Compartment menu, the chemical species menu, the visualization menu, the reaction menu and the Boolean gates menu.

## The menu

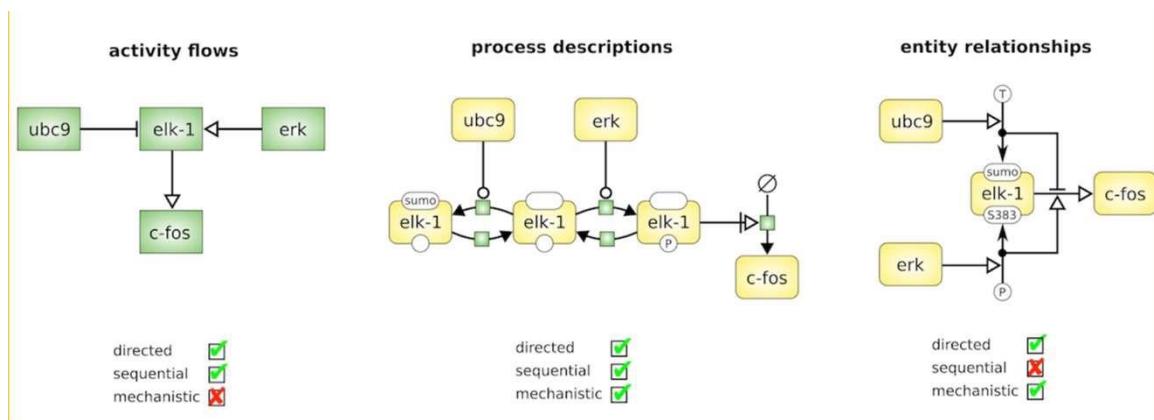


Compartment menu  
Chemical species menu  
Visualization menu  
Reaction menu  
Boolean logic menu

Here is a summary of all schemas that can be used to create your diagram:  
The software suite can accommodate different SBGN schemes such as Process Description or Activity Flow diagrams.

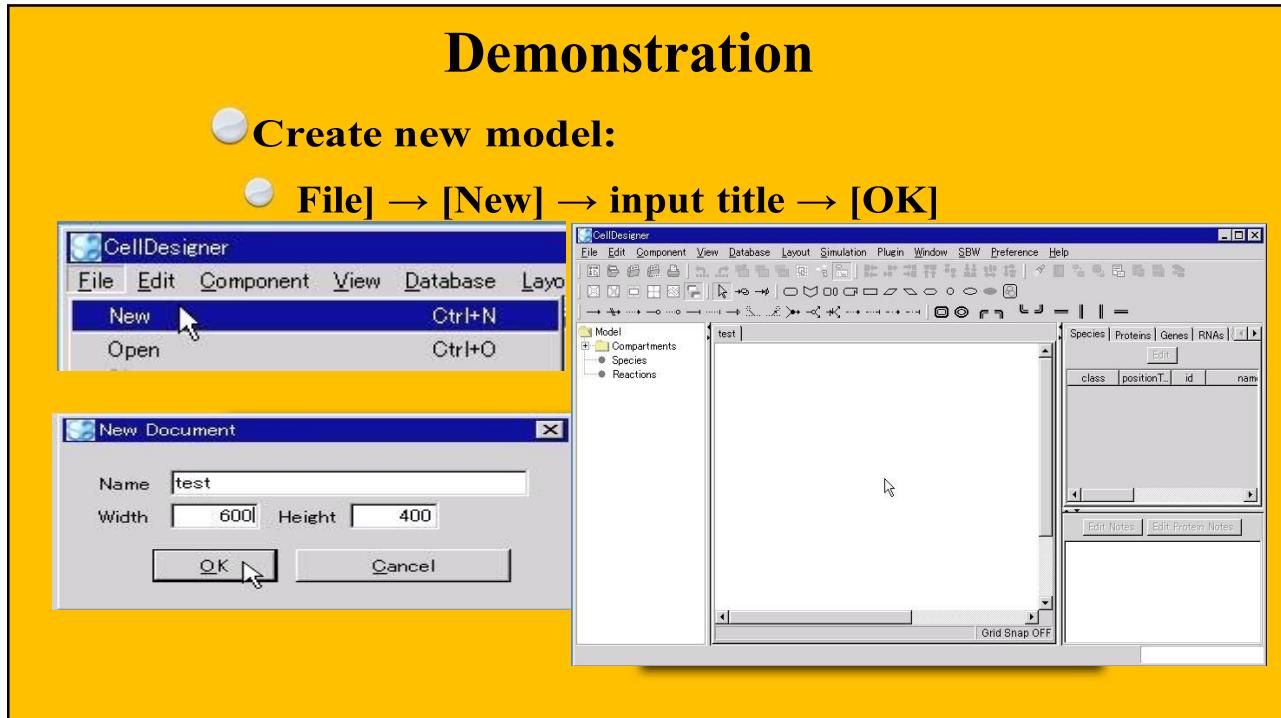


Can you make some comments about the reduced notation scheme? Here are the three different languages of SBGN to help you understand better.

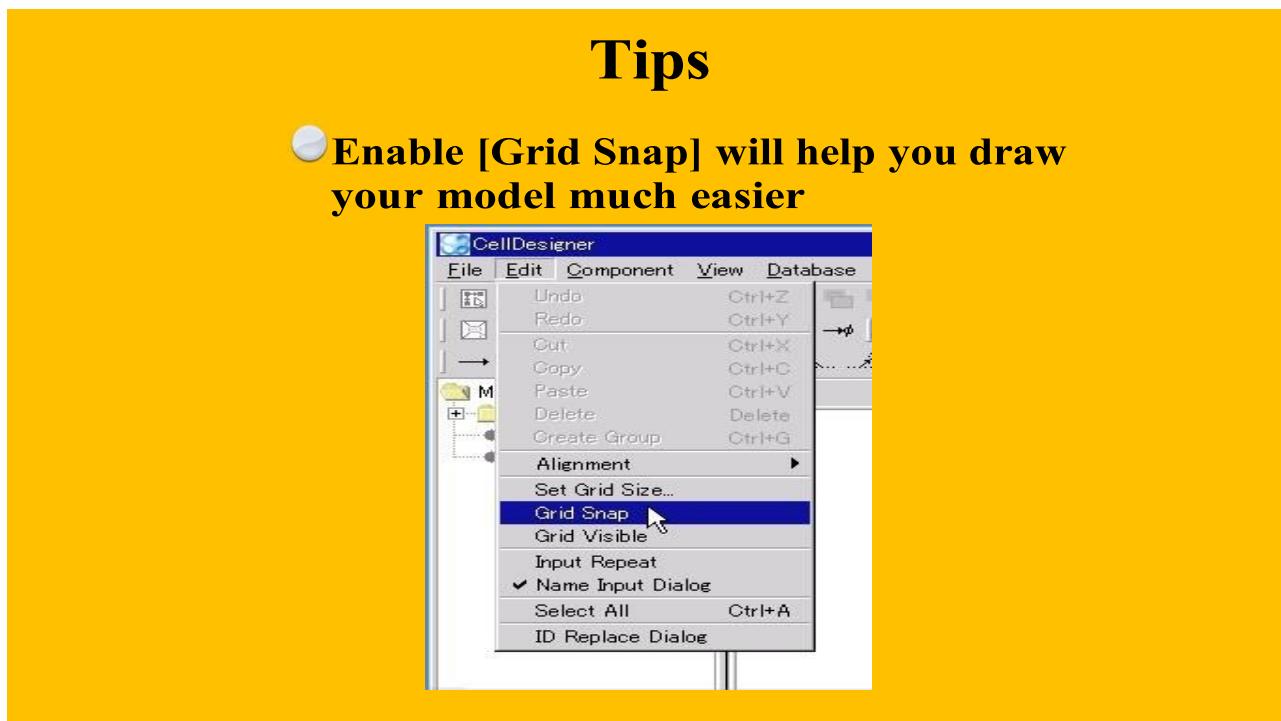


Let's start creating a diagram!

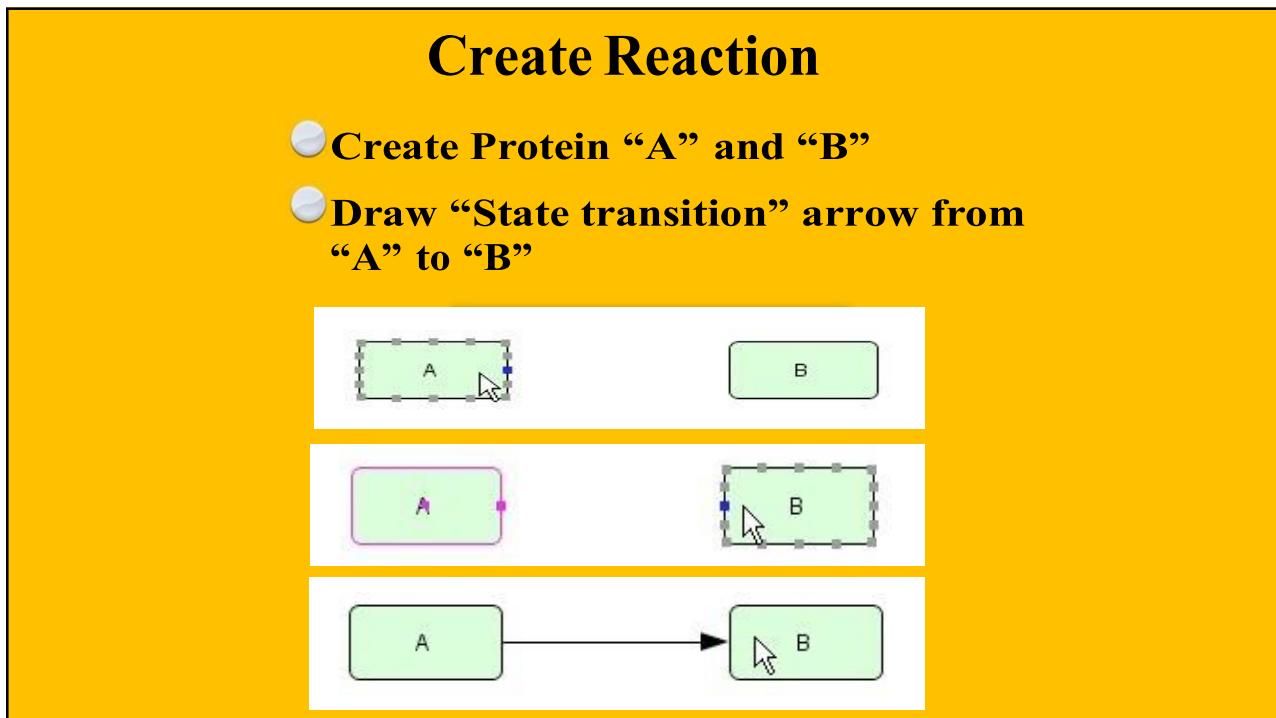
Click on File, then New, then write the title: test and click OK. We will use the default size settings.



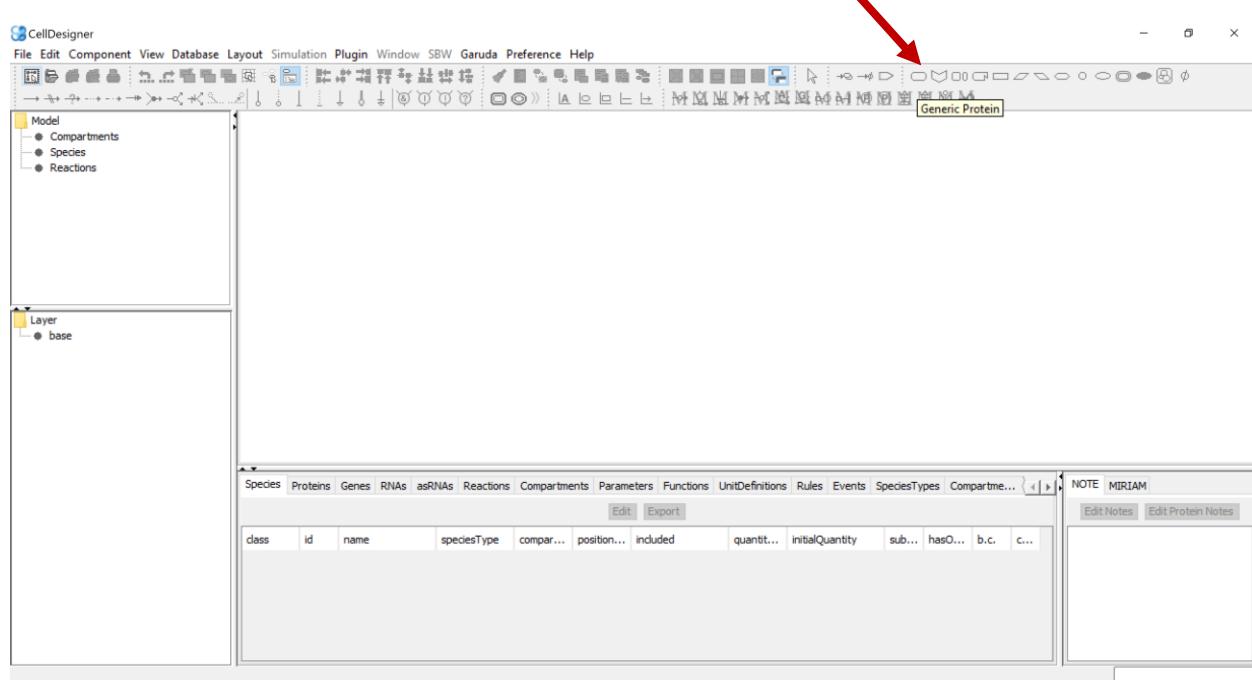
We will also enable the grid to help us draw more aligned diagrams. To do so, we will click on Edit in the Menu bar and then on Grid Snap as seen in the screenshot below:



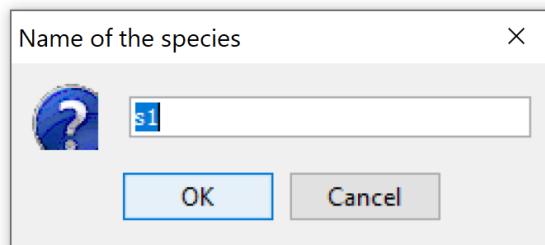
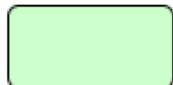
Now we are ready to create our first reaction!



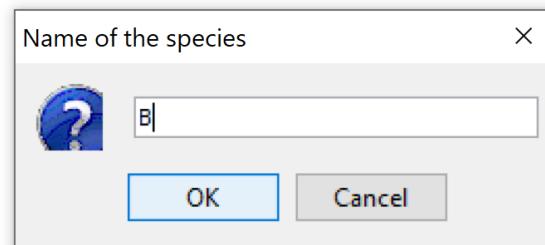
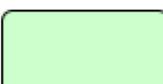
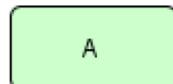
Choose from the glyph menu a generic protein :



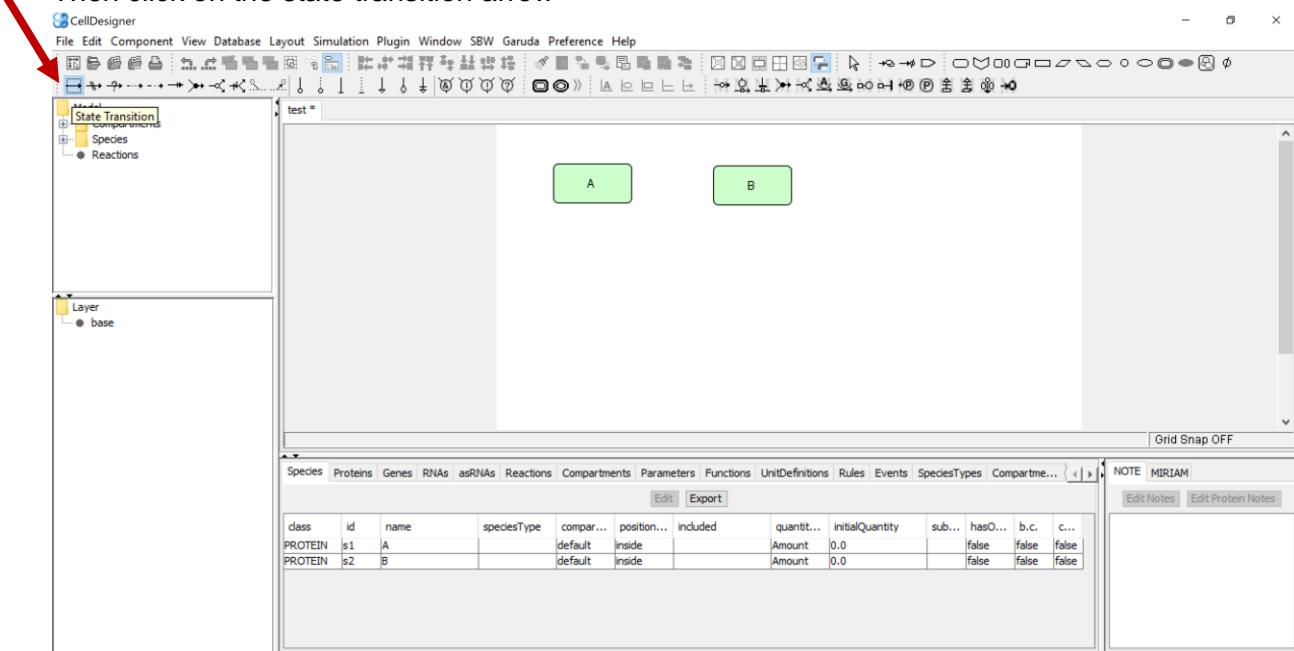
and then click on the window of the drawing space. Name the protein A.



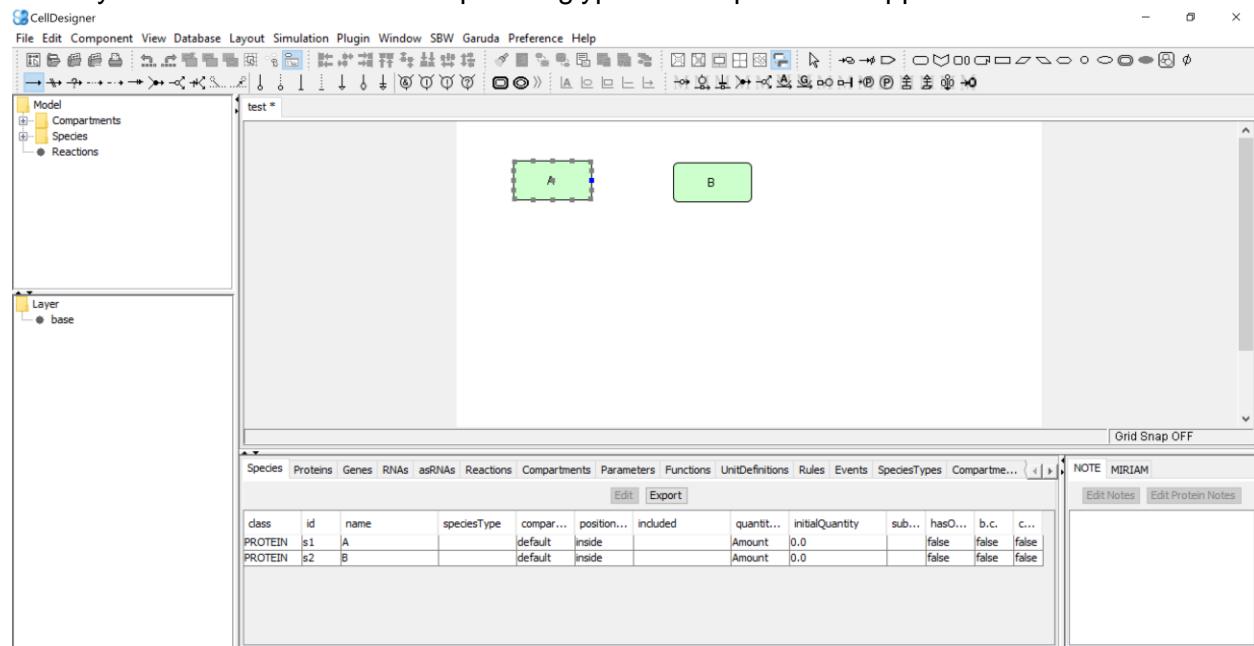
Repeat and name the protein B:



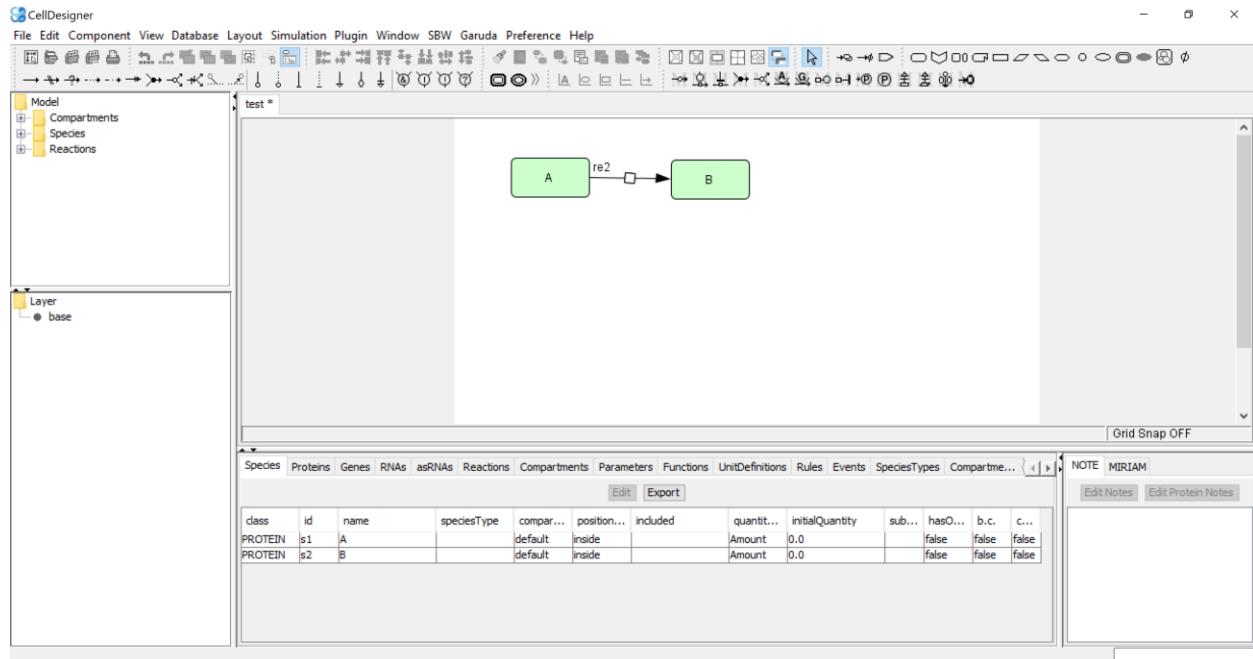
Then click on the state transition arrow



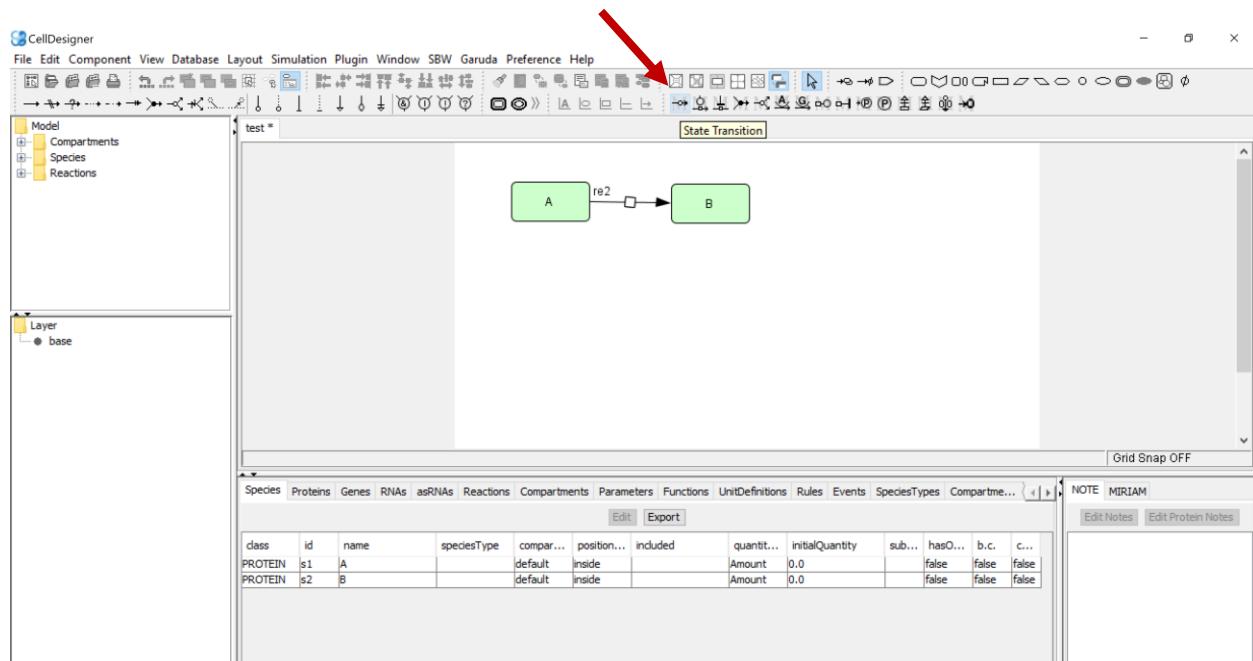
When you move the cursor on the protein glyph anchor points will appear.



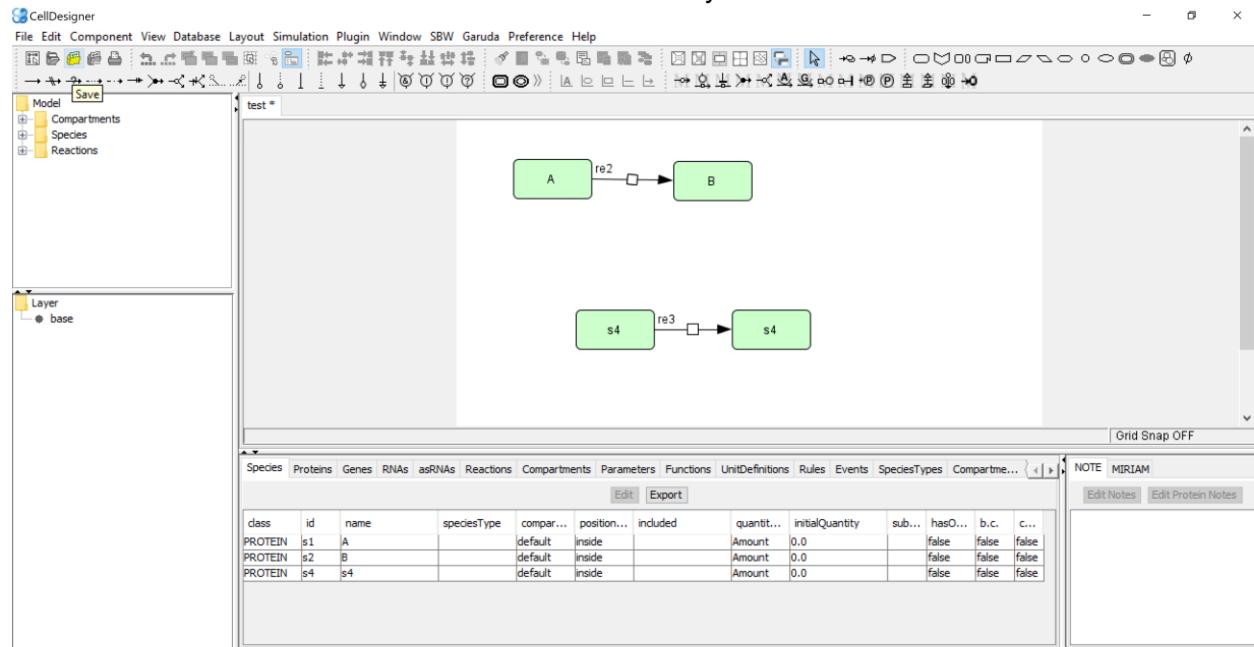
Choose the middle on the right on protein A, click and then choose the middle on the left of protein B and click again to have your arrow drawn.



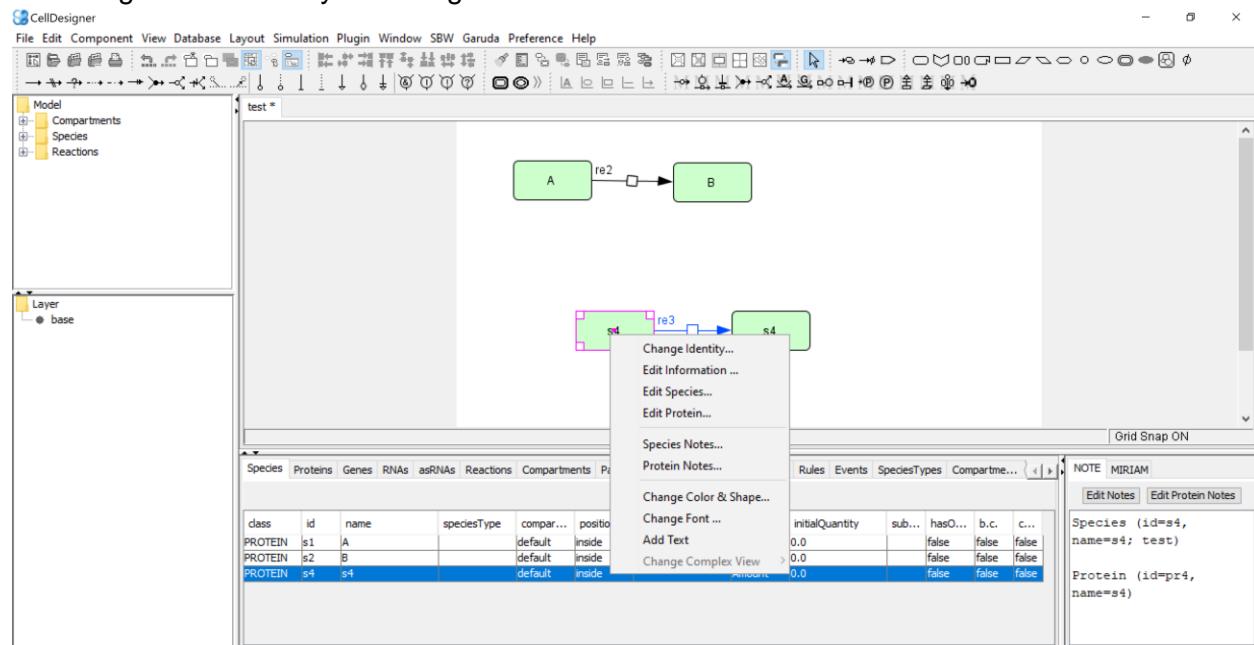
Notice that you can use macros to draw this reaction automatically. Choose the state transition from the macros menu and then click on the drawing space just below the reaction you created:



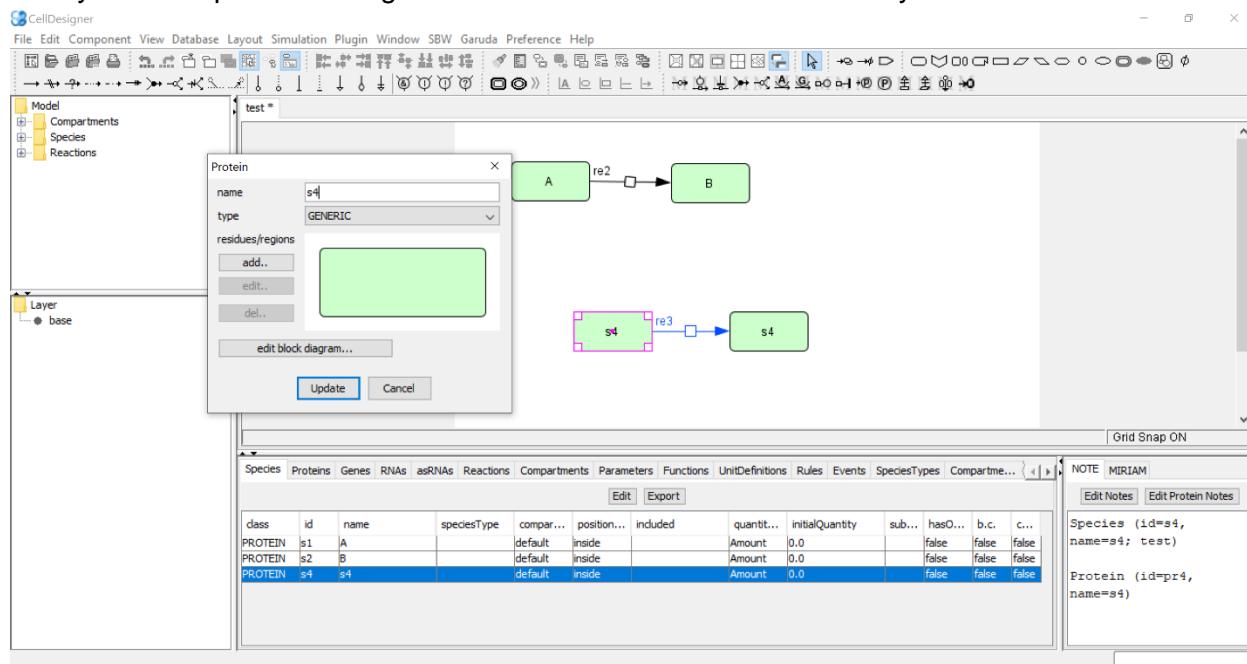
A state transition reaction is now created automatically:



To change their names you can right click on them and choose from the menu Edit Protein



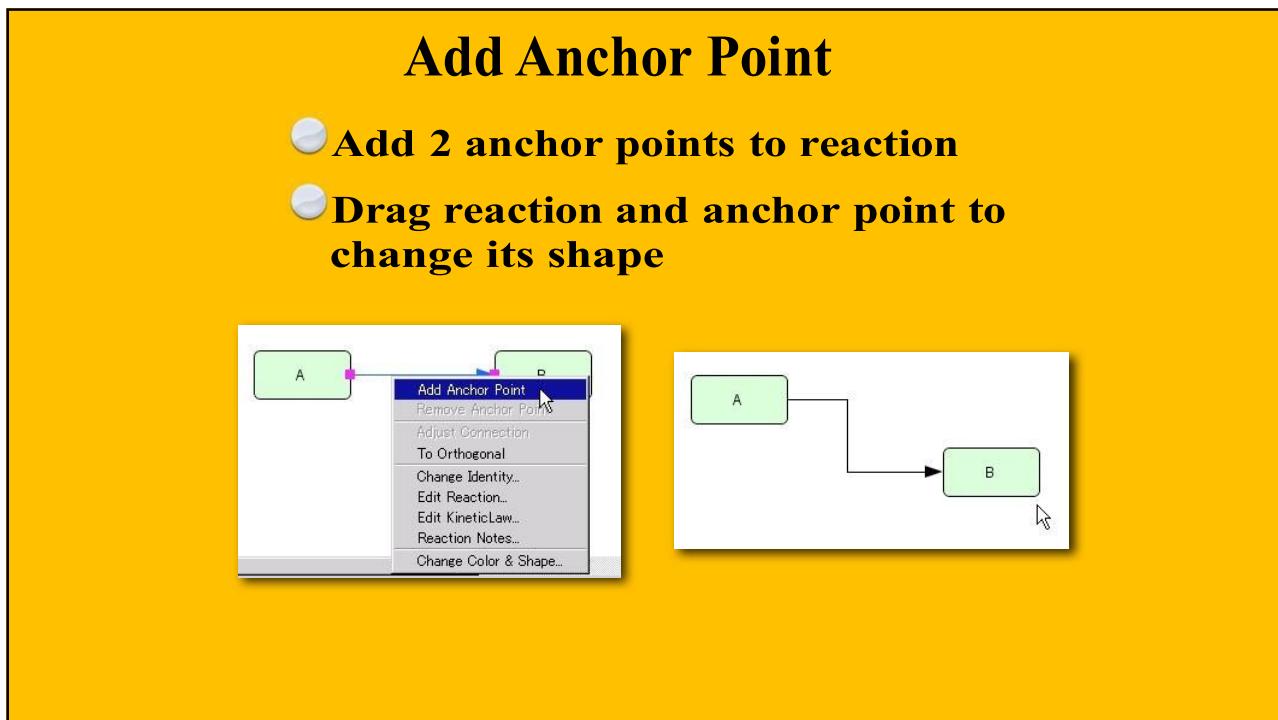
Now you can replace the s4 generic name with C or whatever name you want. You can name it



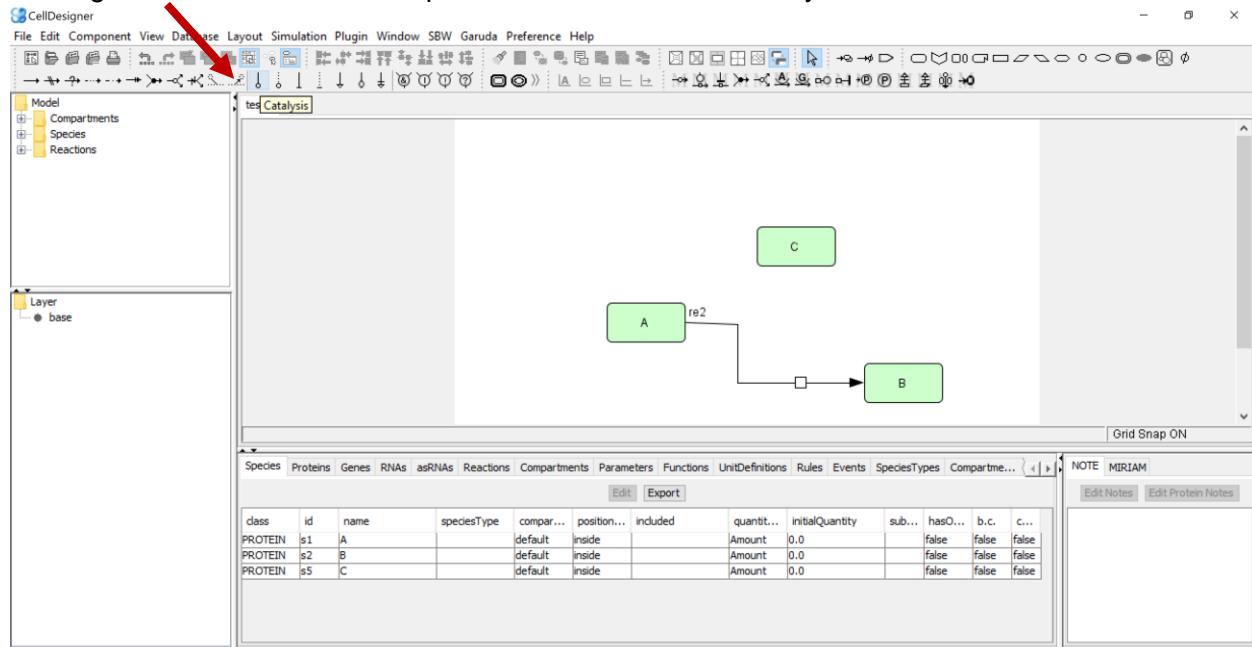
IL6.

What do you observe?

We can also add anchor points:

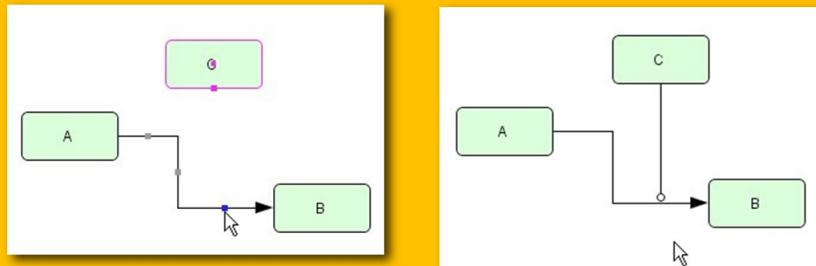


Now let us try to add a protein that has a positive effect (catalyzes) the reaction we created previously. We would need to select a generic protein, click on the drawing space, and then change its name. The next step would be to select the catalysis arrow and add it:



## Add Catalysis reaction

- ➊ Add Protein “C”
- ➋ Add Catalysis reaction from “C” to the reaction



In CellDesigner you can use dots to indicate an active state, however, this notation is not used in SBGN language

**Set Active state**

- Select Protein “B”
- [Component] → [SetActive]

The screenshot shows the CellDesigner interface. A context menu is open over a protein labeled 'B'. The 'SetActive' option is highlighted. The menu also includes other options like 'Change Identity...', 'Edit Species...', etc. Below the menu, there is a diagram with three components: 'A' (green rectangle), 'C' (green rectangle), and 'B' (pink rectangle). Component 'A' has a solid arrow pointing to component 'B'. Component 'C' has a solid arrow pointing to component 'B'. To the right of the diagram, there is a smaller version of the same diagram where component 'B' is now represented by a green rectangle with a dashed border, indicating it is active.

You can also change the color by right clicking on the element.

**Change Color**

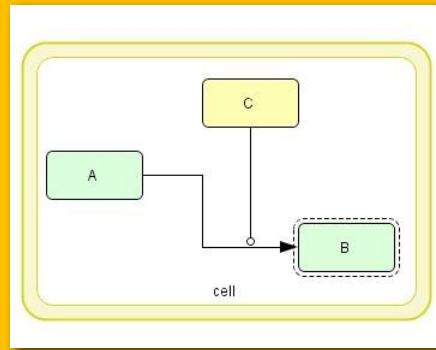
- Right click on Protein “C”
- Select [Change Color & Shape...]

The screenshot shows the CellDesigner interface. A context menu is open over a protein labeled 'C'. The 'Change Color & Shape...' option is highlighted. The menu also includes other options like 'Change Identity...', 'Edit Species...', etc. Below the menu, there is a diagram with three components: 'A' (green rectangle), 'C' (yellow rectangle), and 'B' (green rectangle). Component 'A' has a solid arrow pointing to component 'B'. Component 'C' has a solid arrow pointing to component 'B'. To the right of the diagram, there is a smaller version of the same diagram where component 'C' is now represented by a yellow rectangle with a dashed border, indicating it is active.

Adding compartments is also important:

## Compartment

- Click [Compartment] icon
- Drag mouse cursor to specify its area
- Input name of compartment

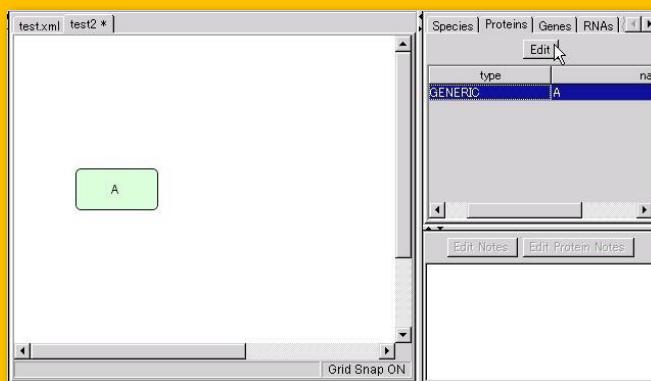


**Practice makes perfect !**

The following exercises in pages 15 – 18 are for practice at home – let's go to page 19 and connect to databases!

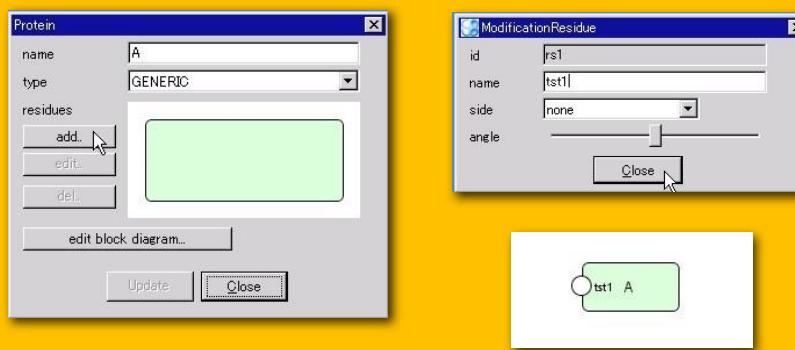
## Add Residue to Protein

- Create new model (test2)
- Create Protein “A”
- Select Protein “A” in [Proteins] Tab
- Click [Edit] button



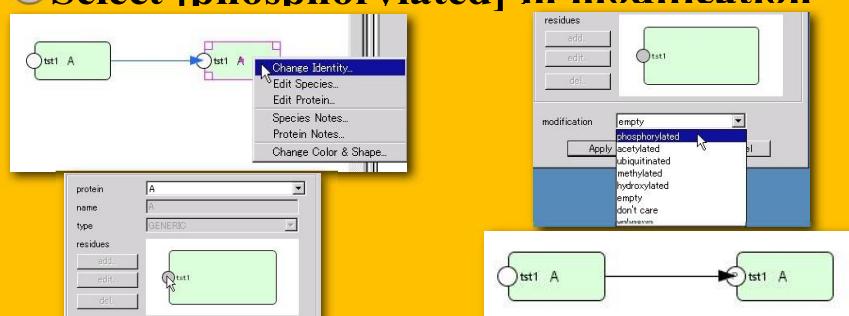
## Add Residue to Protein

- Click [add] button on [Protein] dialog
- Input name for the residue (tst1)
- Click [Close] button
- Click [Update] Button



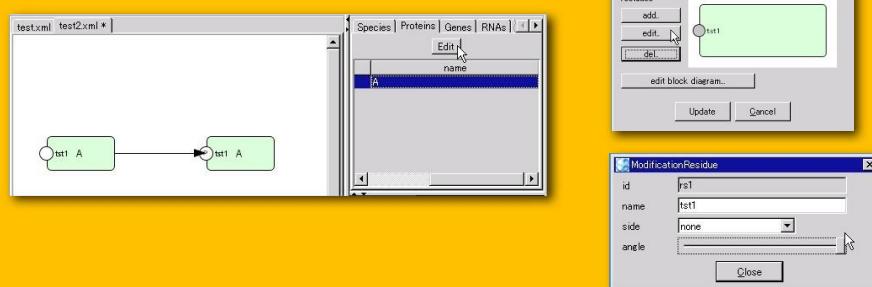
## Add Residue to Protein

- Copy & Paste Protein “A” and then draw “State Transition” arrow
- Right Click on “A” (right side) and select [Change Identity.].
- Click residue “tst1” in Dialog
- Select [phosphorylated] in modification



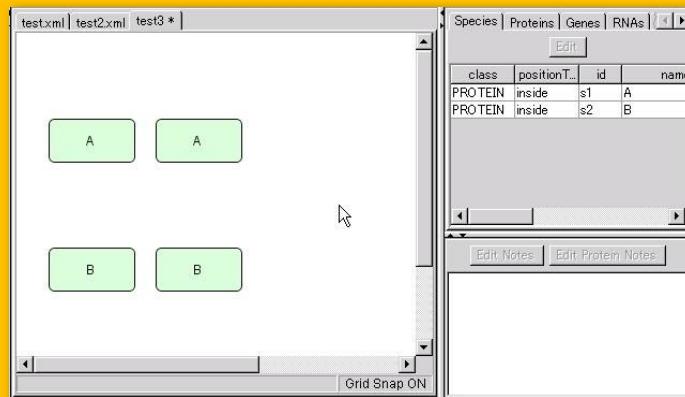
## Change position of Residue

- Select Protein “A” in [Proteins] Tab
- Click [Edit] button
- Click residue “tst1” in Dialog
- Click [edit] button
- Drag [angle] sidebar



# Complex

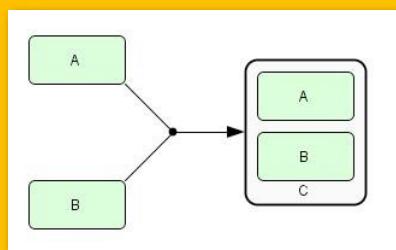
- Create new model (test3)
- Create Proteins “A” and “B”
- Copy & Paste both “A” and “B”



# Complex

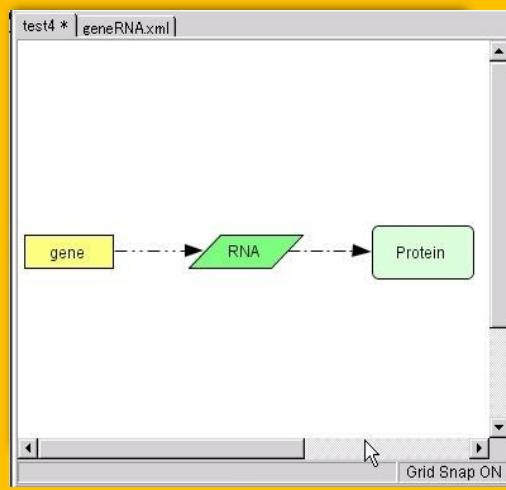
- Click [Complex] icon and create complex “C”  

- Drag Protein “A” and “B” into complex C
- Draw “Association” arrow



## Gene & RNA

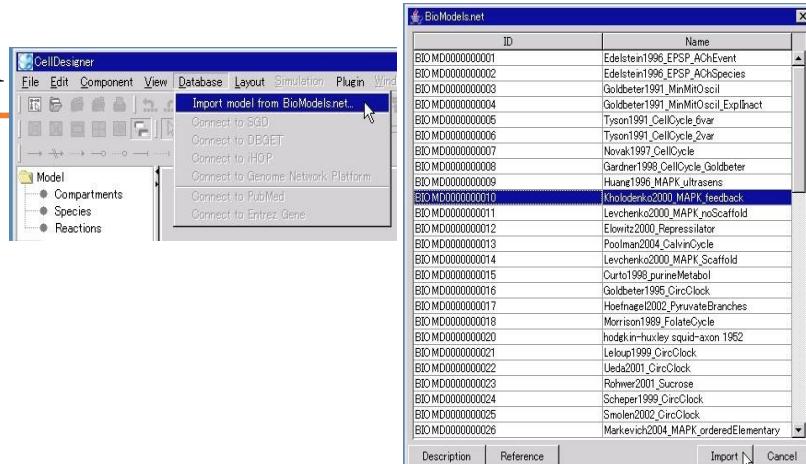
- Create new model (test4)
- Create gene, RNA and Protein
- Draw “Transcription” and “Translation”



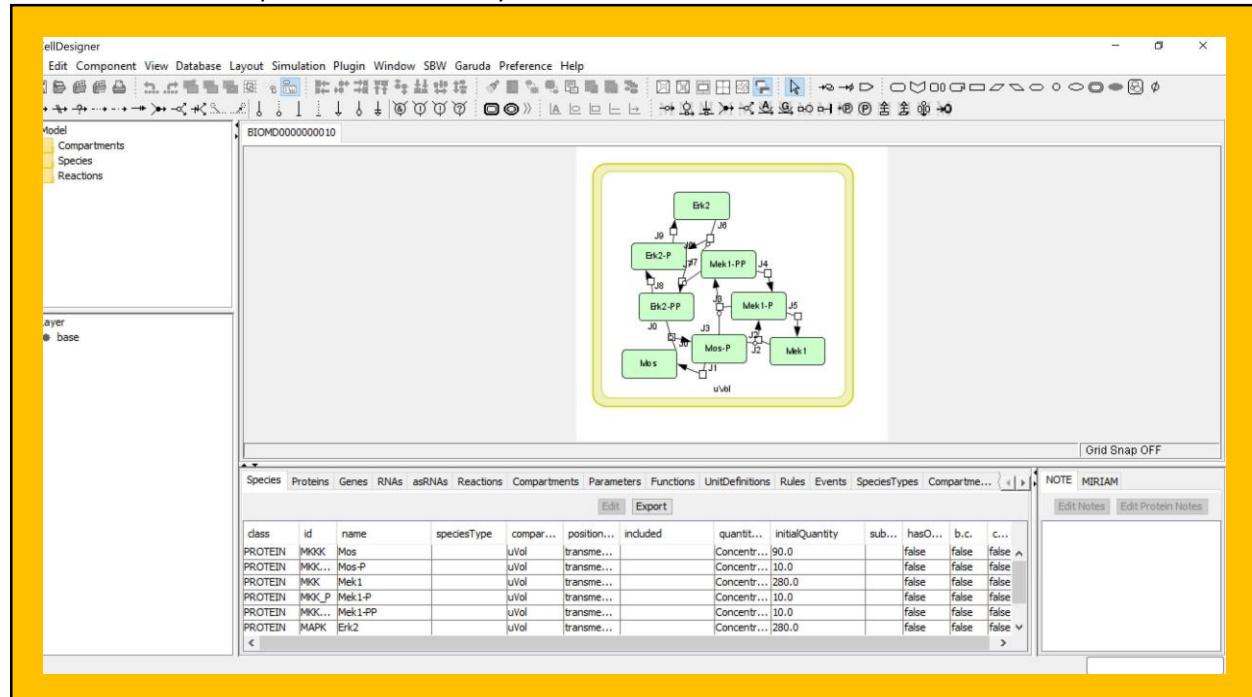
Welcome! Let's see how we can import a model from a database! Start from a clean slate! Create a new model (File, New etc). Then click on the Database tab of the Menu and select a model from BioModels. Here we have selected the MAPK model of Kholodenko (Ultrasensitivity).

# Database Connection

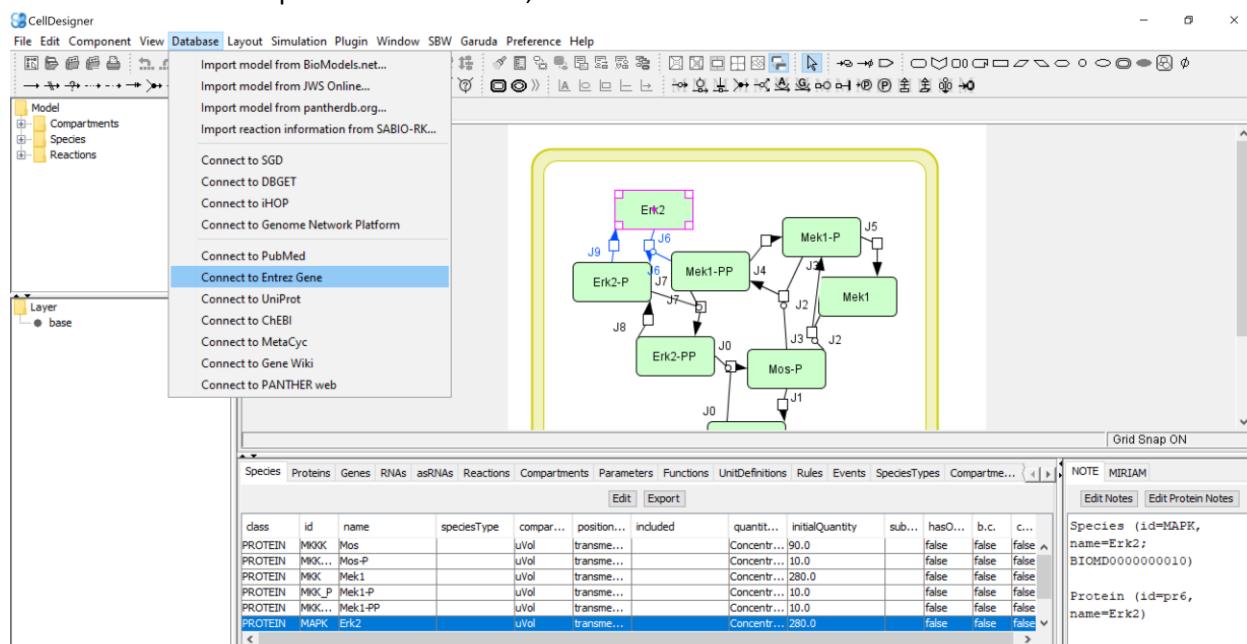
Import model from BioModels.net



The model is then imported automatically! Take some time to observe it!



Now click on the ERk2 protein of the model, then click on Databases and select Connect to Entrez Gene

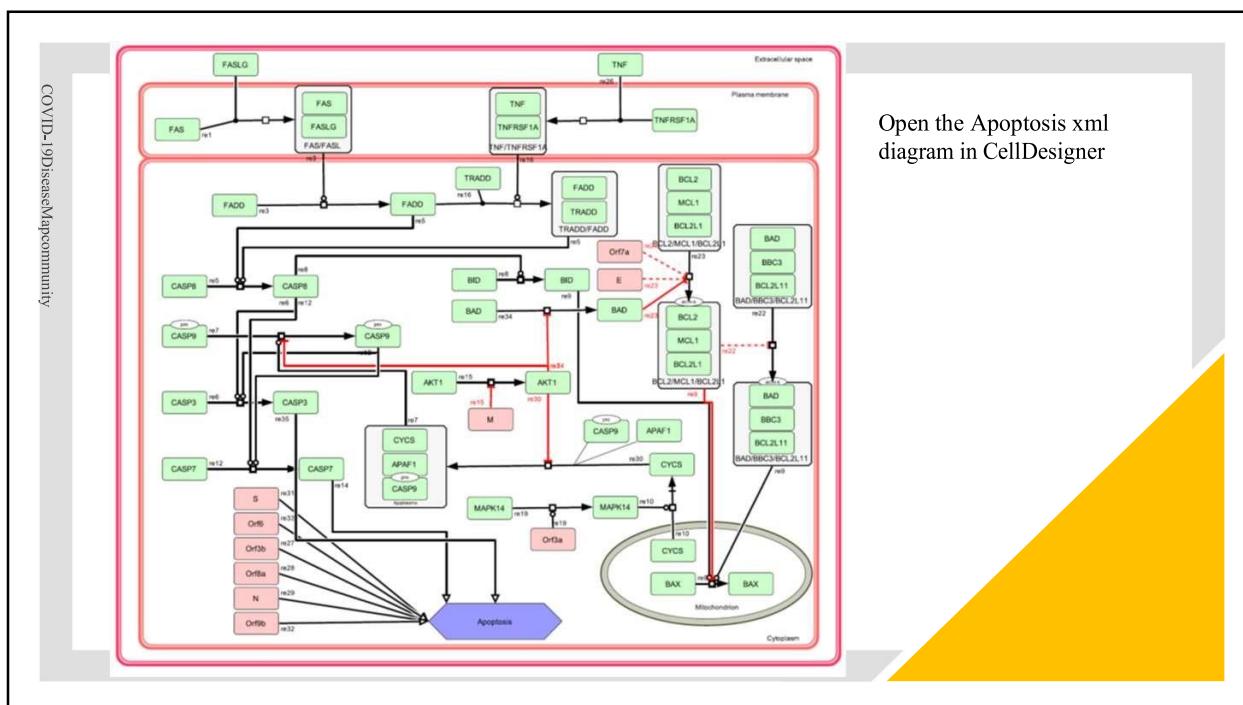
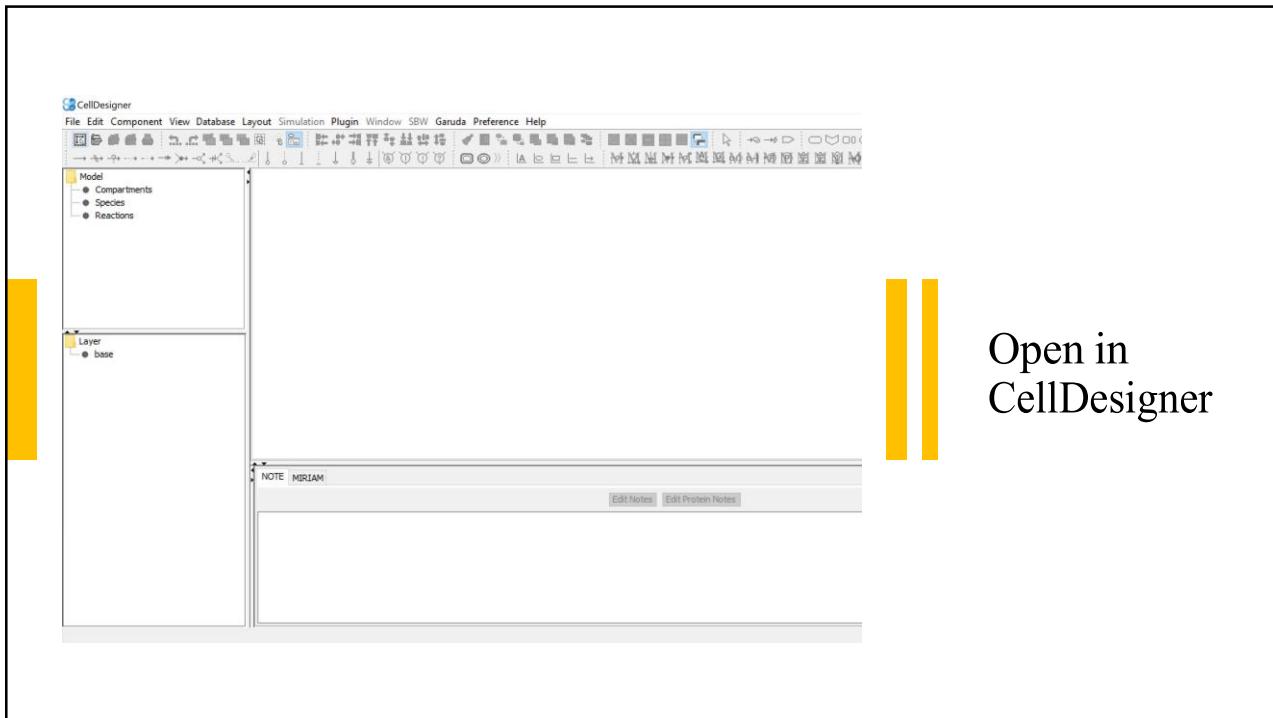


A browser page will open and you will be transferred to the Entrez Gene database site:

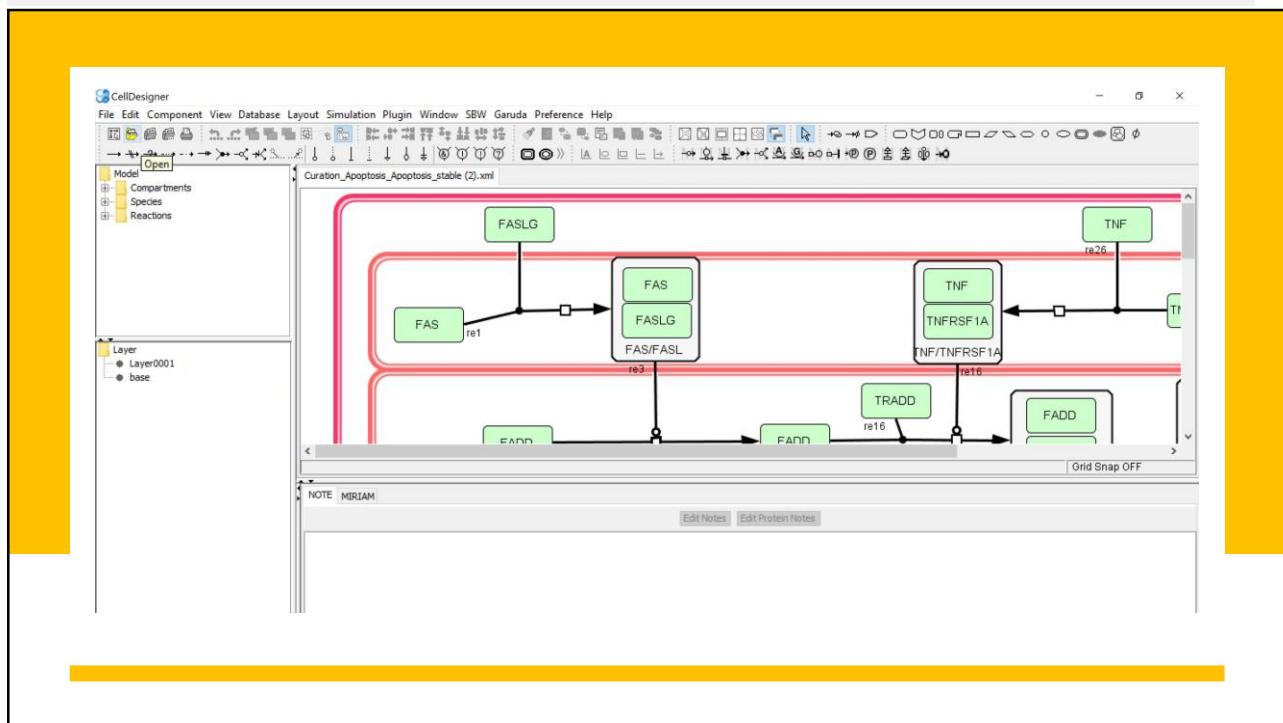
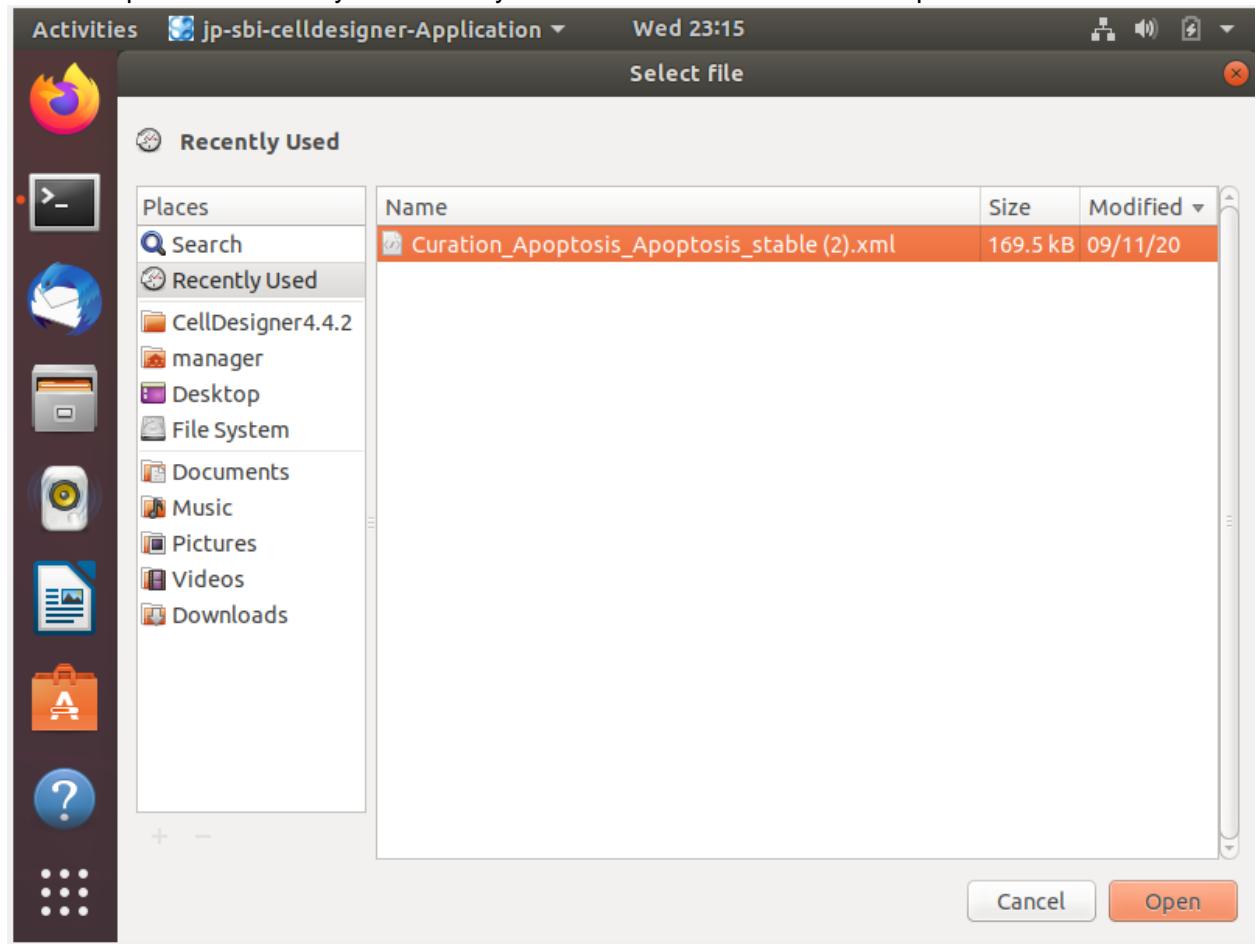
The screenshot shows the NCBI Entrez Gene search results for 'Erk2'. The search bar at the top has 'Gene' selected and 'Erk2' entered. The results table shows one entry for MAPK1 (ERK2) mitogen-activated protein kinase 1. The right side of the page includes filters for 'Manage Filters', 'Results by taxon' (Top Organisms: Homo sapiens, Mus musculus, Rattus norvegicus), and 'Find related data'.

Name/Gene ID	Description	Location	Aliases	MIM
MAPK1 ID: 5594	mitogen-activated protein kinase 1 [Homo sapiens (human)]	Chromosome 22, NC_000022.11 (21759657..21867680)	ERK, ERK-2, ERK2, ERT1, MAPK2, NS13, P42MAPK, PRKM1, PRKM2, p38, p40, p41, p41mapk, p42-MAPK	176948

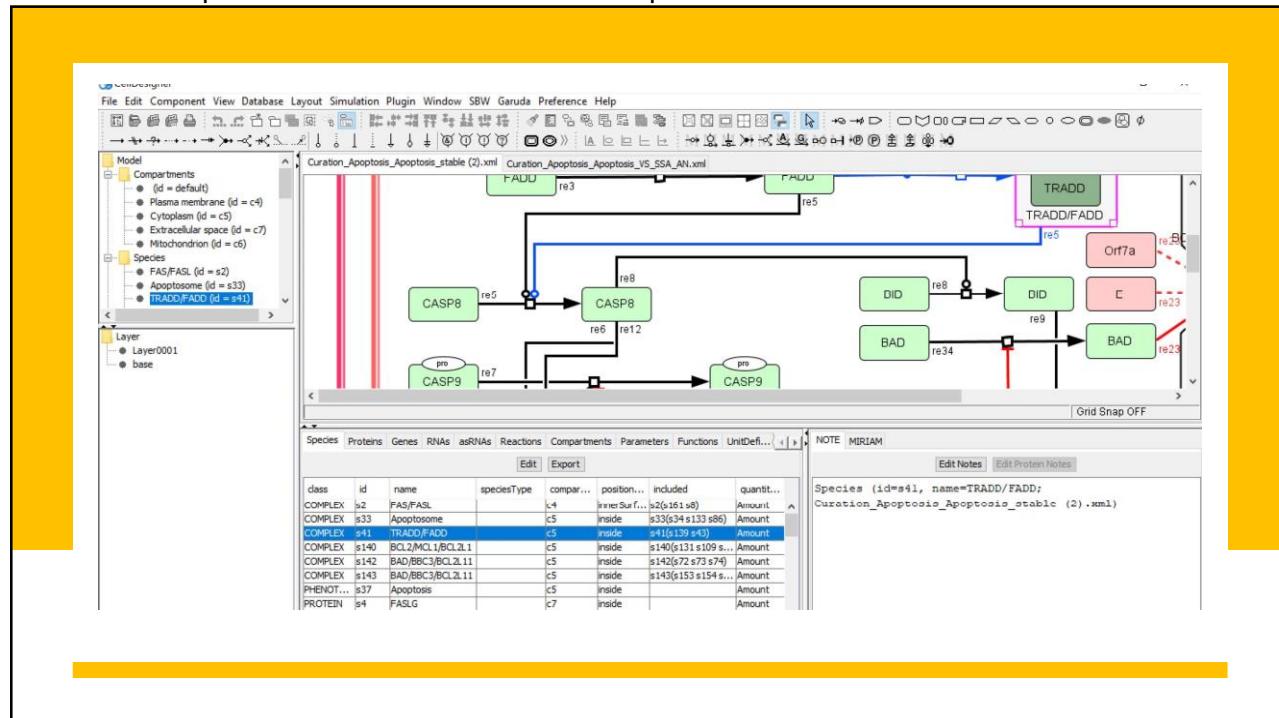
Bonus! Open in CellDesigner the xml file of the Apoptosis module form the COVID19 Disease Map repository. Take some time to observe the layout, the compartments, the species, the annotations. Click on elements and then connect to Entrez Gene or Pubmed to find relevant information!



File-> Open and search your directory to find the file! Here is an example:



Click on a complex to see the information in the species tab



Click on a reaction to see the MIRIAM annotations!

